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HIGHLY SELECTIVE BASE-CATALYSED ADDITIONS OF NITROMETHANE TO LEVOGLUCOSENONE

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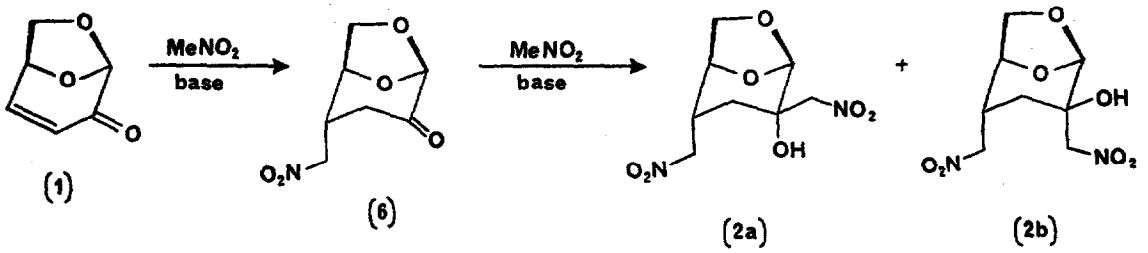
Summary: *Nitromethane undergoes base-catalysed addition to levoglucosenone affording 2:1 and 1:2 adducts (2) and (7) in high yield (≥ 95%); the products result from initial Michael addition exclusively at the exo-face of the alkene* anti *to the 1,6-anhydro bridge.*

Levoglucosenone (1)[1] is a cellulose-derived α,β-unsaturated bicyclic ketone which is attracting widespread current interest as a chiral source of both carbohydrate[3] and non-carbohydrate[4] derivatives. Of particular note is the degree of face selectivity shown for reactions in which it acts as the target for Michael additions[5] and as the 2π-component in Diels Alder[6] and 1,3-dipolar[7] cycloadditions. Attack usually takes place from the less hindered *exo-face anti* to the 1,6-anhydro bridge. We now report that levoglucosenone undergoes highly selective base-catalysed reactions with nitromethane yielding 2:1 or 1:2 adducts depending on reactant ratio.

Treatment of levoglucosenone with an excess of nitromethane (1:48) at 15-20°C in the presence of a catalytic amount of 1,1,3,3-tetramethylguanidine (TMG) afforded a mixture of two isomeric 2:1 adducts in a combined isolated yield of 98%. From their analytical and spectroscopic properties[8] the adducts were identified as *exo,endo*-di(nitromethyl) compound (2a, 89%) and its *exo,exo*-isomer (2b, 9%). No other levoglucosenone-derived products were detected.

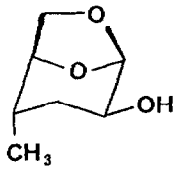


Scheme 1

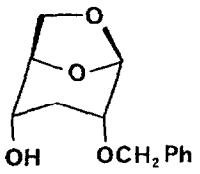
The conformations of the adducts were deduced from their H n.m.r. data by comparison with literature values[9,10] for related compounds (3)-(5) (Table). In both cases the pyranose ring adopts the expected chair-like arrangement. The small coupling (1 Hz) between H(4) and H(5) is consistent only with the nitromethyl group at C(4) being axial and *exo* to the 1,6-anhydro bridge. The alternative structure with H(4) axial would give substantially greater couplings to both H(5) and H(3a). For compound (2a) assignment of the configuration at C(2) was made by comparison of the $^{3}J_{CH}$ couplings between H(3a) and the carbons of the nitromethyl groups [C(9) and C(10)]. The observed value for H(3a)-C(9) of 2.8 Hz strongly supports the proposed *gauche* arrangement with the nitromethyl substituent at C(2) equatorial.[11] In contrast the coupling between H(3a) and C(10) of the nitromethyl group at C(4), which is known to be axial, is 9.1 Hz as expected for a *trans*-diaxial arrangement.

The reaction pathway presumably involves initial Michael addition at C(4) by the nitronate anion ($^{-}CH_2NO_2$) exclusively from the less hindered *exo*-face to form 1:1 adduct (6) (Scheme 1). Subsequent base-catalysed addition of a second nitromethane to the carbonyl group at C(2) affords (2a) and (2b) with lower although significant selectivity (10:1), the major product resulting from *endo*-attack.

(3)



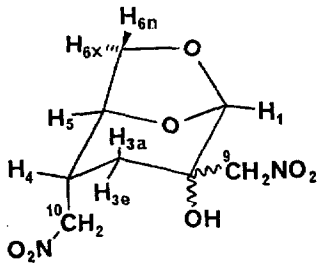
(4)



(5)

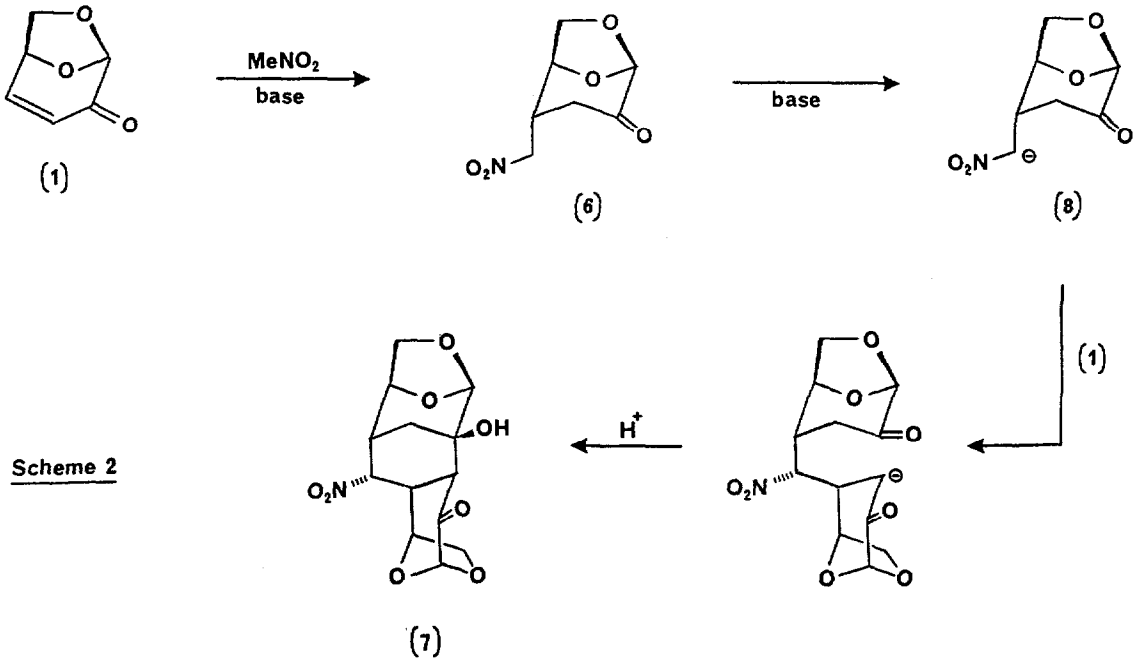
Having established that 2:1 addition products are formed when nitromethane is used as solvent, the reaction was repeated with levoglucosenone in excess. A solution of nitromethane and levoglucosenone (1:2) in 1,2-dichloroethane was stirred with TMG (catalytic amount) at 0-20°C for 4 hours. From the reaction mixture was isolated a white crystalline solid. Elemental analysis and mass spectrometry (*m/z* 313) indicated that it was derived from two molecules of levoglucosenone and one of nitromethane.[12] The detailed structure was established by X-ray crystallography[13] as pentacyclic compound (7). The proposed mechanism for its formation (Scheme 2) involves Michael addition to levoglucosenone of the nitronate anion (8) resulting from removal of a proton at C(10) of the initial 1:1 adduct (6), followed by intramolecular nucleophilic addition to the carbonyl group at C(2). The high isolated yield (95%) shows that every step in the series of additions is highly selective; in each case attack occurs exclusively at the *exo*-face.

Table ^{1}H n.m.r. coupling constants (Hz)[a]



Compound	1,3e	3a,3e	3a,4	3e,4	3e,5	4,5	5,6n	5,6x	6n,6x
(2a)[b]	1.5	15.3	6.9	1.5	1.5	0.9	1.0	5.4	7.7
(2b)[c]	-	15.2	7.4	1.6	-	<1	0.9	5.4	7.7
(3)[d]	-	14.9	6.9	1.5	-	2.0	2.0	4.0	-
(4)[e]	-	12.8	6.1	1.5	-	2.0	2.0	4.0	-
(5)[e]	-	-	~4.5	<1.5	-	2.8	0.8	5.4	7.7

(a) Spectra recorded in CD_3COCD_3 at 360 MHz; (b) other couplings: *1,4* ~1, *4,10a* 8.1, *4,10b* 6.1, *9a,9b* 11.6, *10a,10b* 13.8 Hz; (c) other couplings: *4,10a* 8.7, *4,10b* 6.4, *9a,9b* 12.0, *10a,10b* 13.8 Hz; (d) ref 9; (e) ref 10.



Scheme 2

Carrying out the reaction under similar conditions with equimolar amounts of nitromethane and levoglucosenone afforded a mixture of the same principal products (2a) and (7) in 61% and 18% yields respectively. These results demonstrate that the Michael addition of nitromethane to levoglucosenone occurs in near quantitative yields with exceptionally high selectivity.

Acknowledgement. We thank the SERC for the award of a studentship (A.C.F).

References and Footnotes

1. Systematic name: 1,6-anhydro-3,4-dideoxy-β-D-*glycero*-hex-3-enopyranos-2-ulose.

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8. 1,6-*Anhydro*-3,4-*dideoxy*-2,4-*di*-C-*nitromethyl*-β-*D*-ribo-*hexopyranose* (2a), m.p. 117-8°C (Et_2O) (Found: C, 38.3; H, 4.8; N, 11.3. $C_8H_{12}N_2O_7$ requires C, 38.6; H, 4.8; N, 11.3%); $[\alpha]_D^{24}$ -72° (c 1.0, EtOH); ν_{max} (Nujol) 3480 (OH), 1560, 1350 cm^{-1} (NO_2); δ_C (50 MHz, $CDCl_3$) 101.2 (C-1), 81.3 (C-9), 76.0 (C-10), 72.8 (C-5), 69.4 (C-2), 66.5 (C-6), 33.9 (C-4), 27.7 (C-3); *m/z* (f.a.b., glycerol) 249 [$(M+1)^+$]. 1,6-*Anhydro*-3,4-*dideoxy*-2,4-*di*-C-*nitromethyl*-β-*D*-arabino-*hexopyranose* (2b), m.p. 107-9°; *m/z* 248 (M^+).

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10. R.H. Furneaux, G.J. Gainsford, F. Shafizadeh, and T.T. Stevenson, *Carbohydr. Res.*, 1986, 146, 113.

11. *Eg* C. Morat, F.R. Taravel, and M.R. Vignon, *Magn. Reson. Chem.*, 1988, 26, 264 and references therein. We thank Drs D. Reed and I.H. Sadler for performing these experiments, details of which will be published in the full paper.

12. 1R,3S,4R,5R,8S,9R,10R,11R,12S-4-*Hydroxy*-10-*nitro*-6,14,15,17-*tetraoxa*-*pentacyclo*[10.2.1.$1^{4,9}$.$1^{5,8}$.$0^{3,11}$]*heptadecan*-2-*one* (7), m.p. 244-5°C (EtOAc) (Found: C, 49.5; H, 4.7; N, 4.5. $C_{13}H_{15}NO_8$ requires C, 49.8; H, 4.8; N, 4.5%); $[\alpha]_D^{24}$ -201° (*c* 1.0, CH_2Cl_2); ν_{max} (Nujol) 3470 (OH), 1725 (C=O), 1545 cm^{-1} (NO_2); *m/z* 313 (M^+).

13. We thank Dr R.O. Gould for the structure determination, details of which will be presented in the full paper.

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